U.S. Food and Drug Administration

Generic Drug User Fee Amendments of 2012

http://www.fda.gov/gdufa

Thomas Hinchliffe, Pharm.D.
CDR, U.S. Public Health Service
Special Assistant to the Director
Office of Generic Drugs
Food and Drug Administration

Disclaimer & Disclosure

- Views presented are those of the speaker and do not reflect official FDA, DHHS or other government opinion or policy.

- I have nothing to disclose.

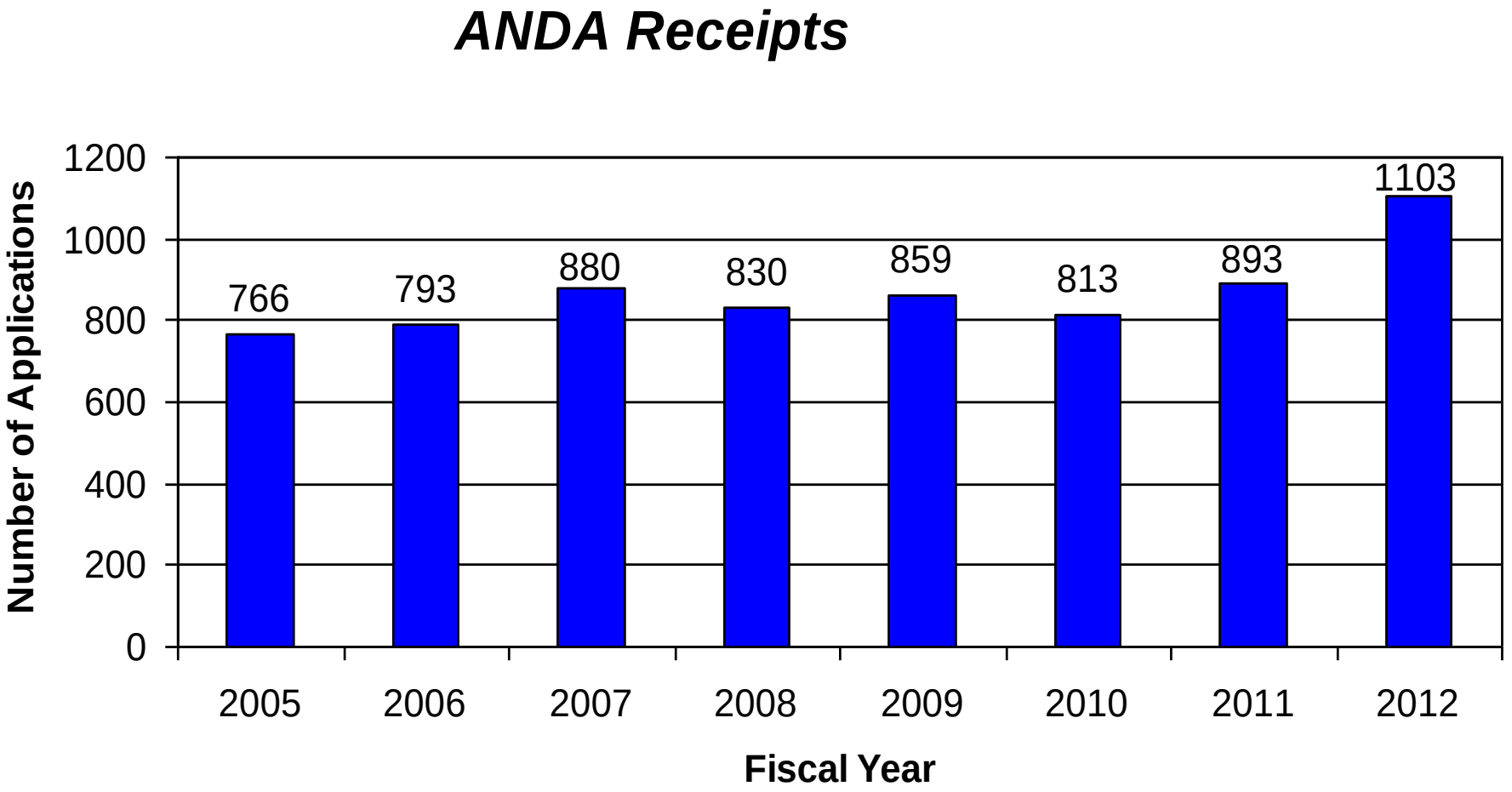
Agenda

- Generic Drug User Fee Amendments of 2012 (GDUFA) Program Overview
- Key Definitions under GDUFA
- Overview of Goals and Metrics
- Complete Response
- Changes to Supplements
- Post 1st Complete Response Teleconference requests

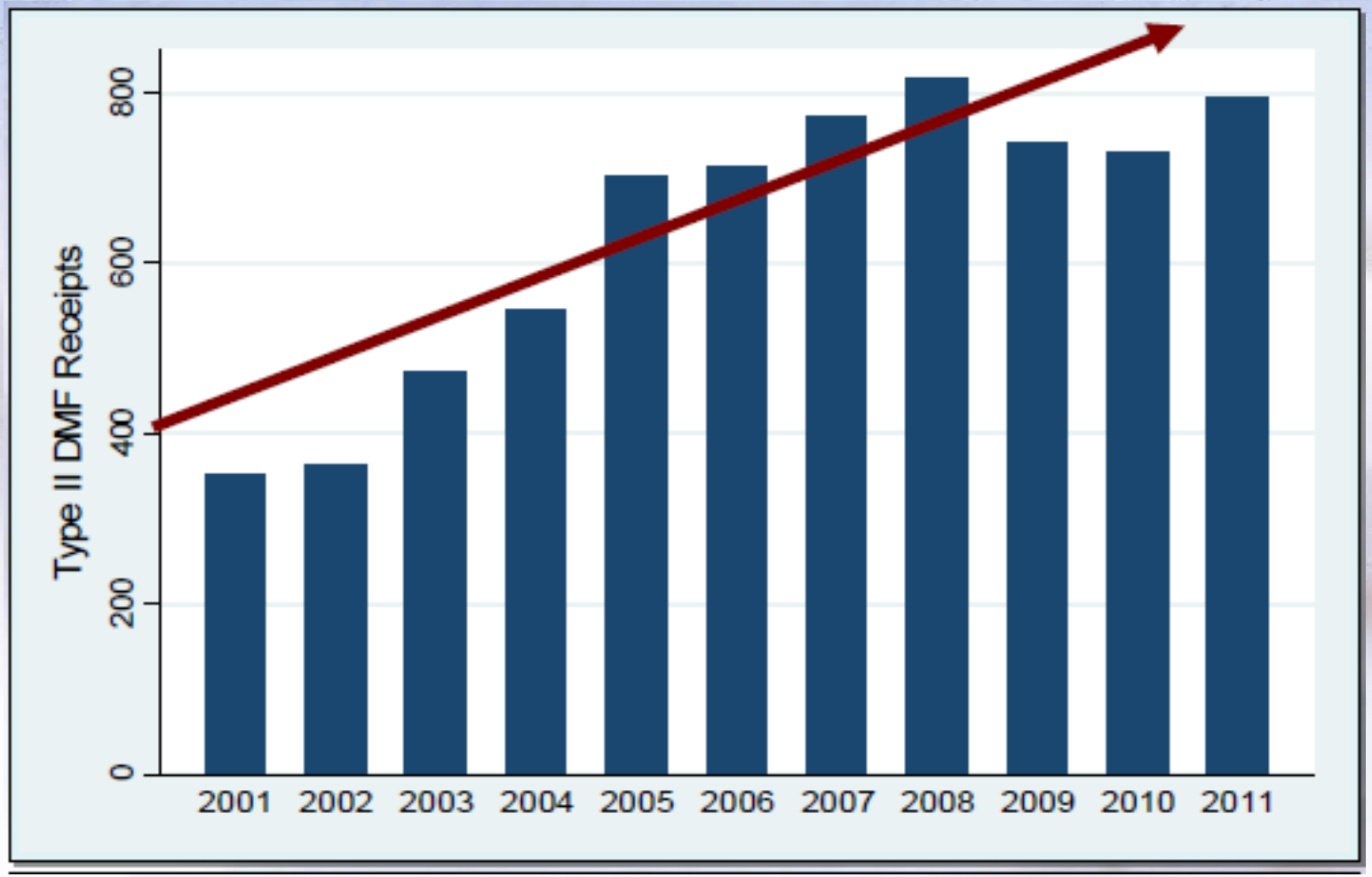
Generic Drug User Fee -Why Now?

- Generics industry success
  - $1.07 trillion in savings (2002-2011)
    - Market growth continues
  - Unprecedented regulatory challenge in terms of Size, Scope, Geography
- Significant growth in ANDA submissions
  - Increasing review times and backlog of applications
  - Increasingly complex products
- Program funding has remained relatively flat

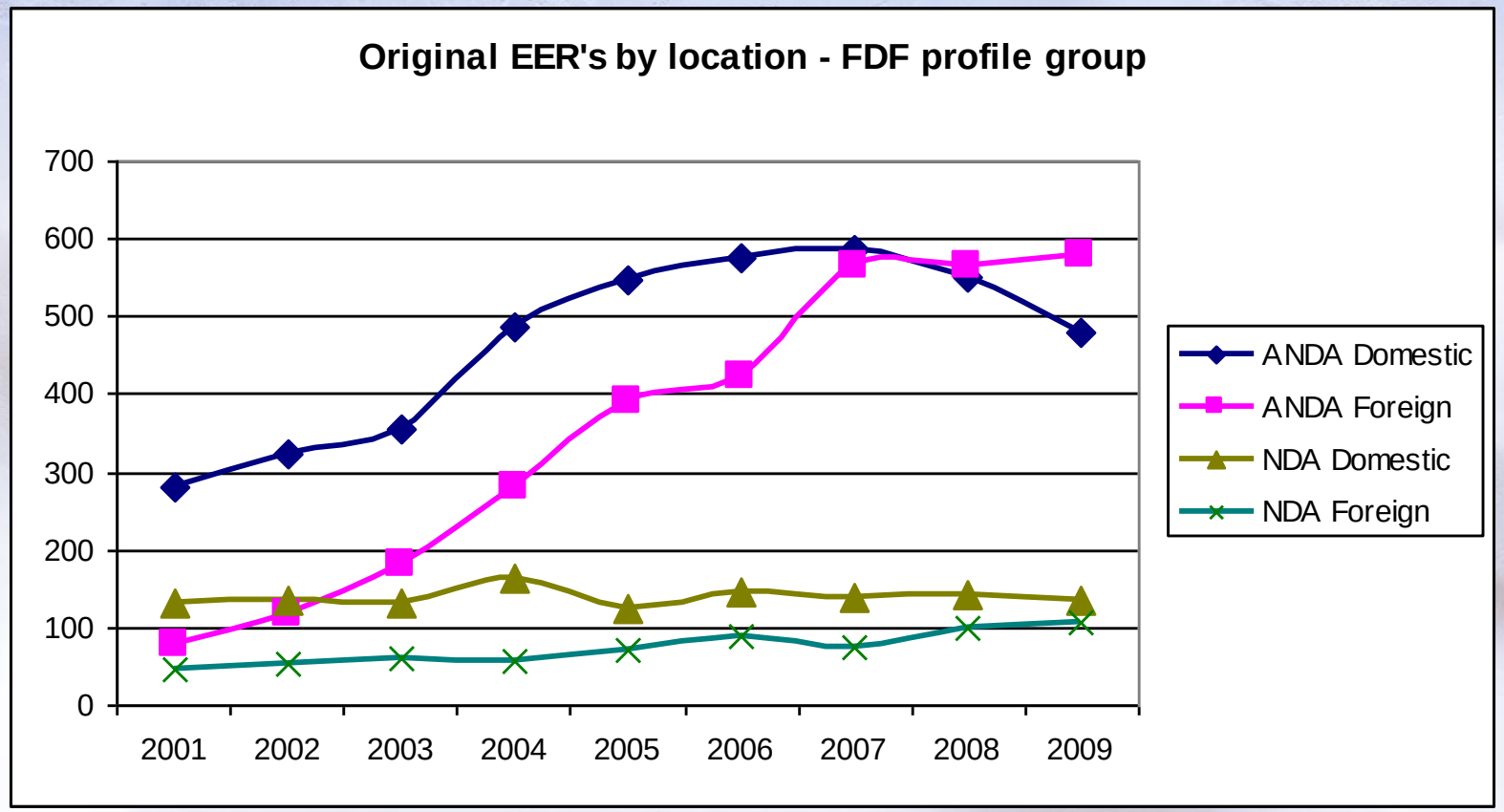
Abbreviated New Drug Application (ANDA) Growth Expected to Continue



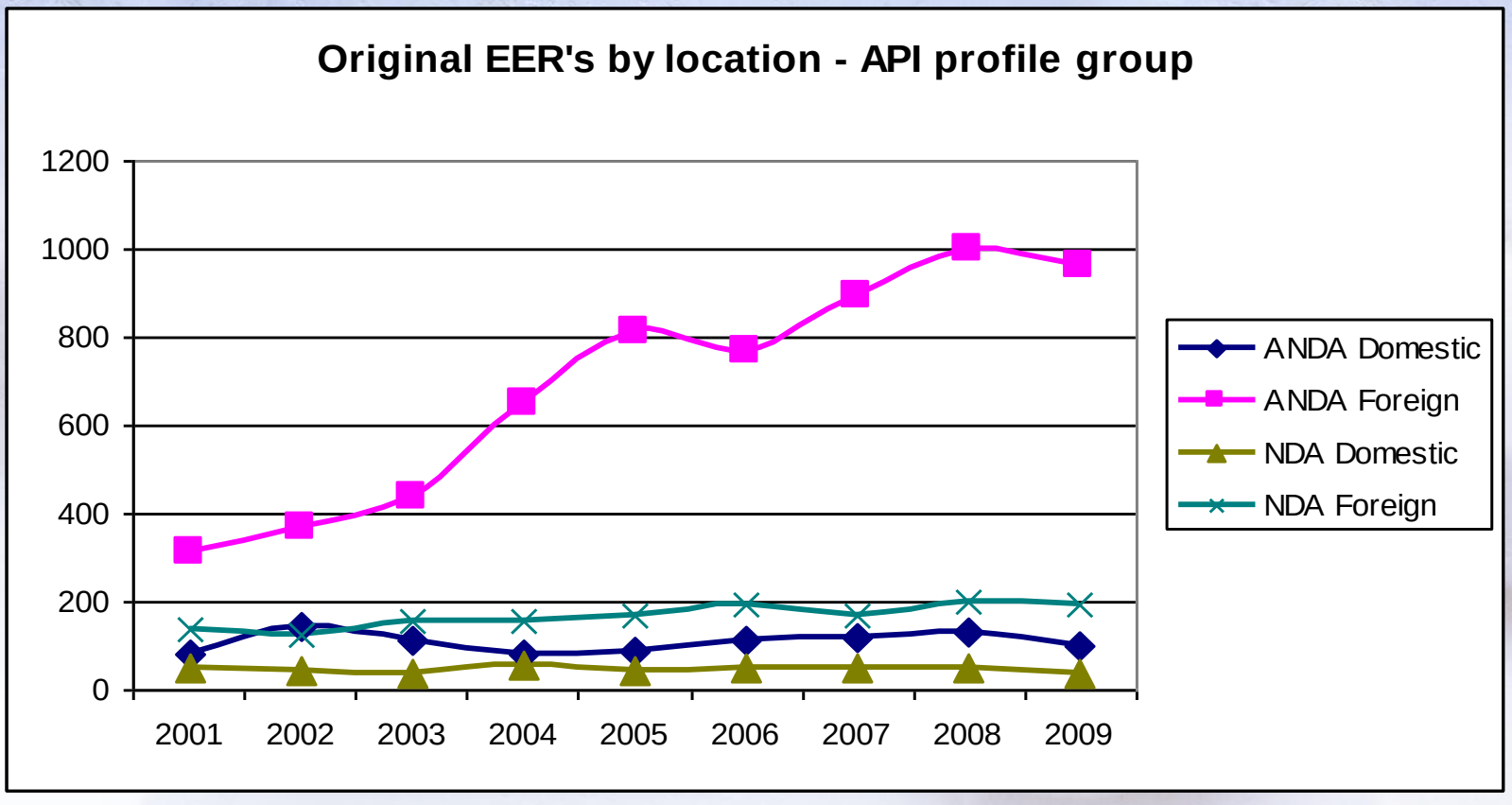
Drug Master Files (DMFs) Also Rapidly Growing



Increases in Finished Dosage Form (FDF) Foreign Inspections



Increases in Foreign API Inspections



Generic Drug Program: Not just OGD

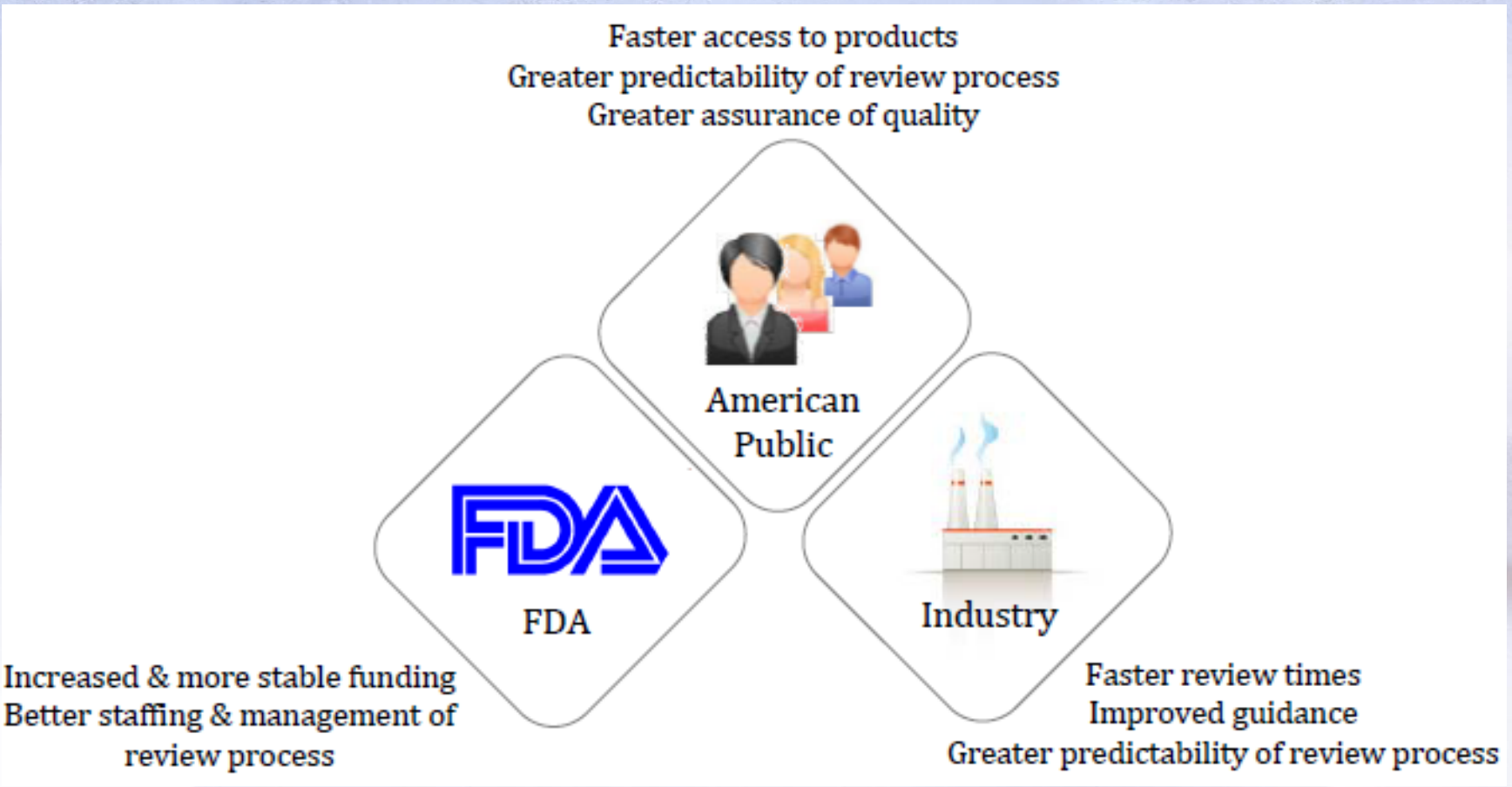
- Involves all of CDER
  - OGD is the interface for ANDA applicants to interact with the Generic Drug Program
- Other FDA units:
  - ORA (the field)
  - CDRH
  - Office of the Commissioner

Generic Drug User Fee Amendments of 2012 (GDUFA)

Key Achievements of GDUFA

- GDUFA advances critical values
  - Timely access to safe, high-quality generic drugs
  - Maintains affordability of generic drugs
  - Increases transparency
  - Addresses globalization
  - Advances regulatory science
  - Expected to put FDA's generic drug program on a stable financial footing

What do FDA, industry and the public get from additive user fees with performance goals?



GDUFA Overview

- 5 Year Program
- $299 million, inflation-adjusted, per year
  - Supplemental resources to FDA
  - Less than ½ of 1% of Generic Drug Sales
  - Less than ten cents for the average generic prescription.
- 4 types of fees: Backlog; DMF; ANDA/PAS; Facility
  - 30% of program revenue from application (ANDA/PAS/DMF)
  - 70% of program revenue from facilities
    - 80% from Finished Drug Form (FDF) Facility
    - 20% from Active Pharmaceutical Ingredient (API) Facility

GDUFA Overview *(Continued)*

FDA commits to program enhancements and performance goals:

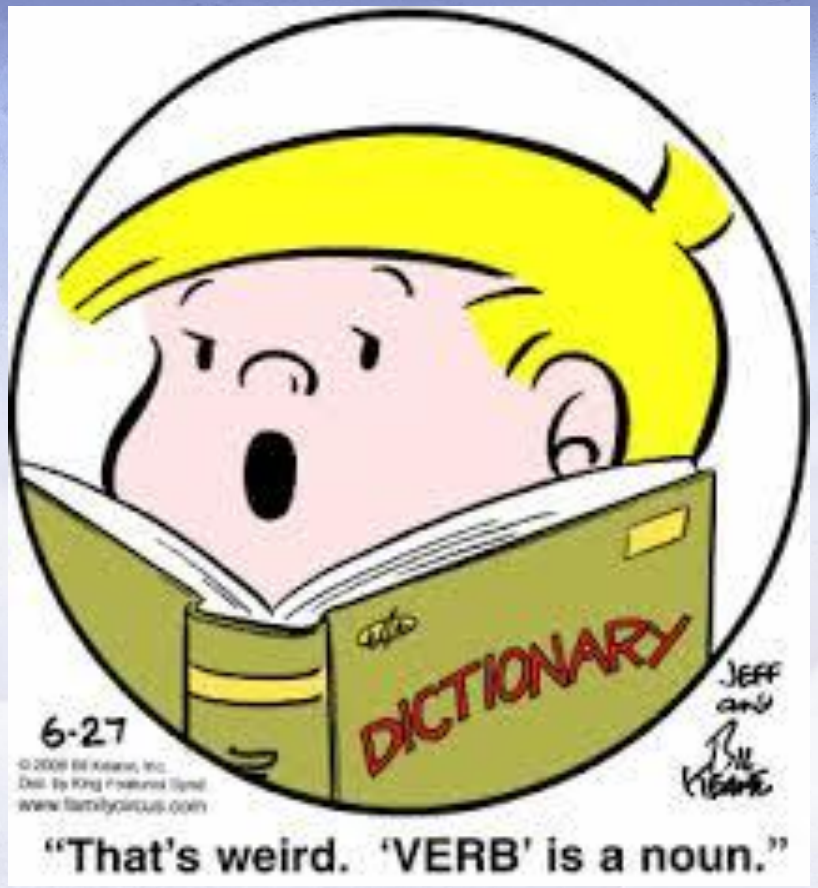
- Efficiency enhancements starting on day one.
- Ten-month review cycle for 90% of applications in year 5.
- Effectively eliminate the backlog within 5 years.
- Risk-adjusted parity of foreign & domestic inspections in year 5.

FDA Commitments:

- Abbreviated New Drug Applications (ANDAs)
  - Complete response (CR) letters
  - Division-level deficiency review
  - Prompt communication of easily correctable deficiencies
  - First cycle post complete response meetings
  - For years 1 and 2 of the program, expedite paragraph IV (Day 1 Submissions)

FDA Commitments:

- Drug Master Files (DMFs)
  - DMF completeness assessment criteria
  - Available for reference list (www.fda.gov/gdufa)
  - Issue complete response letters
  - Provide division-level deficiency reviews
  - Promptly communicating easily correctable deficiencies
- Inspections
  - Release inspection classification and date
  - Third-party foreign regulator inspection program evaluation



Definitions under GDUFA

Definitions under GDUFA*

- **Act on an application** - means FDA will either issue a complete response letter, an approval letter, a tentative approval letter for an ANDA, or a refuse to receive action.

- **Backlog** – refers to the pending ANDAs, ANDA amendments and ANDA Prior Approval Supplements that have not received a minimum of a Tentative Approval as of October 1, 2012.

- **Complete review** – refers to a full division-level review from all relevant review disciplines, including inspections, and includes other matters relating to the ANDA and associated DMFs as well as consults with other agency components.

* From Generic Drug User Fee Act Program Performance Goals and Procedures

Definitions under GDUFA *(continued)*

- **Complete response letter -** refers to a written communication to an applicant or DMF holder from FDA usually describing all of the deficiencies that the agency has identified in an abbreviated application (including pending amendments) or a DMF that must be satisfactorily addressed before the ANDA can be approved. Complete response letters will reflect a complete review and will require a complete response from industry to restart the clock.
  - If a citizen petition raises an issue that would delay only part of a complete response, a response that addresses all other issues will be considered a complete response

Definitions under GDUFA *(continued)*

- **Cohort** – The program is structured based on 5 cohorts of submission dates (original ANDAs, PASs and DMFs), corresponding to the five fiscal years to be covered by the program.
  - Year 1 cohort - submissions in FY 2013 (Oct 1, 2012 to Sept 30, 2013)
  - Year 2 cohort - submissions in FY 2014 (Oct 1, 2013 to Sept 30, 2014)
  - Year 3 cohort - submissions in FY 2015 (Oct 1, 2014 to Sept 30, 2015)
  - Year 4 cohort - submissions in FY 2016 (Oct 1, 2015 to Sept 30, 2016)
  - Year 5 cohort - submissions in FY 2017 (Oct 1, 2016 to Sept 30, 2017)

Definitions under GDUFA *(continued)*

- **Delaying amendments** – refers to amendments to an ANDA from the ANDA sponsor to address actions by a third party that would cause delay or impede application review or approval timing and that were not or may not have been initially recognized by FDA as necessary when the application was first submitted.
  - FDA's Office of Generic Drugs has been given broad discretion to determine what constitutes a delaying event caused by actions generally outside of the applicants control taking into account facts and information supplied by the ANDA sponsor.

Definitions under GDUFA *(continued)*

- Active Pharmaceutical Ingredient (API):
  - a substance, or a mixture when the substance is unstable or cannot be transported on its own, intended to be used as a component of a drug and intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the human body; or
  - a substance intended for final crystallization, purification, or salt formation, or any combination of those activities, to become the final active pharmaceutical ingredient as defined in paragraph (A).

Definitions under GDUFA *(continued)*

- Finished Dosage Form (FDF):
  - a drug product in the form in which it will be administered to a patient, such as a tablet, capsule, solution, or topical application;
  - a drug product in a form in which reconstitution is necessary prior to administration to a patient, such as oral suspensions or lyophilized powders; or
  - any combination of an active pharmaceutical ingredient, as defined in paragraph (m)(2), with another component of a drug product for purposes of production of such a drug product.

Goals and Metrics

Goals and Metrics of GDUFA

- What is a Goal?
  - This is an actual date on the calendar that requires a certain action to be taken by FDA prior to it expiring.

- What is a Metric?
  - A reportable percentage of the work that is expected to be completed prior to the GDUFA listed goal date.

Metrics

- Backlog:
  - Review and act on 90% of backlog ANDA's and PAS's pending on October 1, 2012, by end of FY 2017

- Original ANDA Review, and Prior Approval Supplement's
  - Review and act on by FY designated goal date
    - 60% of submissions for year 3 cohort (FY15)
    - 75% of submissions for year 4 cohort (FY16)
    - 90% of submissions for year 5 cohort (FY17)

Metrics *(continued)*

- Amendments (review and act on by FY designated goal date):
  - 60% of submissions for year 3 cohort
  - 75% of submissions for year 4 cohort
  - 90% of submissions for year 5 cohort

- Controlled Correspondence
  - 70% of controlled correspondence responded to in FY 2015
  - 70% of controlled correspondence responded to in FY 2016.
  - 90% of controlled correspondence responded to in FY 2017.

Goals – Originals

- **Backlog (Pre-Oct 1) ANDAs:**
  - Goal: Action (AP, TA, CR, WD, RTR) by October 1, 2017

- **Cohort Year 1 and 2 (FY13 and FY 14) submitted Original ANDAs :**
  - No goal defined in GDUFA

- **Cohort Year 3 and 4 (FY15 and FY16) submitted Original ANDAs:**
  - 1st cycle review CR issued in 15 months

- **Cohort Year 5 (FY 17) submitted Original ANDAs:**
  - 1st cycle review CR issued in 10 months

Goals – Prior Approval Supplements

- **Backlog (Pre-Oct 1) PASs:**
  - Goal: Action (AP, TA, CR, WD, RTR) by October 1, 2017

- **Cohort Years 1 and 2 submitted PASs:**
  - No goal defined in GDUFA

- **Cohort Year 3 thru 5 (FY15, FY16, and FY17) submitted PASs:**
  - If requires inspection - 1st cycle review CR issued in 10 months
  - No inspection Required - 1st cycle review CR issued in 6 months

Goals - Amendments

- **Background**
  - All amendment goals are incremental, and the time periods specified are calculated from the date of submission.
  - Added to the original review goal, but will not shorten the original goal date. (ie. an amend with a 6 month clock which was submitted 4 months prior to original goal date would add 2 months to the review clock).
  - An amendment pre Complete Response Letter adjusts the goal date for the original application.
    - Subsequent amendments pre Complete Response Letter also adjust the goal date for the application and are additive.
  - An amendment post Complete Response Letter sets a new goal date for the application.
    - Subsequent amendments post Complete Response Letter also adjust the goal date for the application and are additive.

Goals – Amendments *(Background continued)*

- Amendments shall be grouped as Tier 1, Tier 2 or Tier 3
- Amendment containing multiple elements (tiers) - longest goal date shall apply
- “Delaying amendments” do not add to the count of amendments but do impact goal date
- Unsolicited amendments submitted that are routine or administrative in nature and do not require scientific review (e.g., requests for final ANDA approval, patent amendments, general correspondence, and USP monograph updates), will not lengthen or impact the original review goal date.

Goals – Amendments (continued)

- **Apply to all Originals and PASs**

- **Tier 1 Amendments: (All Cohorts)**
  - All solicited first major and the first five minor amendments.
  - All unsolicited amendments indicated by sponsor and agreed by FDA to be a result of either delaying actions (delaying amendments)

Tier 1 Amendment requiring new Compliance Insp.	**10 month goal**
1st Major Amendment to CR	**10 month goal**
1st thru 3rd Minor Amendment to CR	**3 month goal**
4th thru 5th Minor Amendment to CR	**6 month goal**

Goals – Amendments (continued)

- **Tier 2 Amendments (All Cohorts):**
  - All unsolicited amendments not arising from delaying actions
  - **GOAL – 12 months from date of submission**

- **Tier 3 Amendments (All Cohorts):**
  - Any solicited major amendment subsequent to the first major amendment
  - Any solicited minor amendment subsequent to the fifth minor amendment
  - **GOAL – No Goal clock started**

Complete Response

Complete Response

- "Starting on October 1, 2012….FDA will issue complete response letters, rather than discipline specific letters, for all ANDAs…"*
- Major paradigm shift
  - FDA, OGD and for industry

* GDUFA Program Performance Goals and Procedures Commitment Letter

Complete Response *(continued)*

- Similarly, ALL responses from Applicants to any outstanding deficiencies must be in the form of a **"*Complete Response Amendment*".**
  - This means the applicant is expected to combine any current outstanding (unaddressed) deficiencies into ONE single amendment.
  - Cover Letter should be labeled **"*Complete Response Amendment*"** and list the disciplines responded to, i.e. CHEMISTRY, LABELING, etc.

Complete Response *(continued)*

- The primary point of contact in OGD should always be the Regulatory Project Manager (RPM)
  - Contacting reviewers, team leaders, division directors, and others in management is ineffective and slows OGD down.
- If applicant is ready to respond to any set of deficiencies, contact the Regulatory Project Manager (RPM) in OGD before sending in a discipline specific amendment, particularly if unaware of other discipline specific review status.
- Submitting your response in piecemeal fashion without instruction may delay your ANDA or supplement!

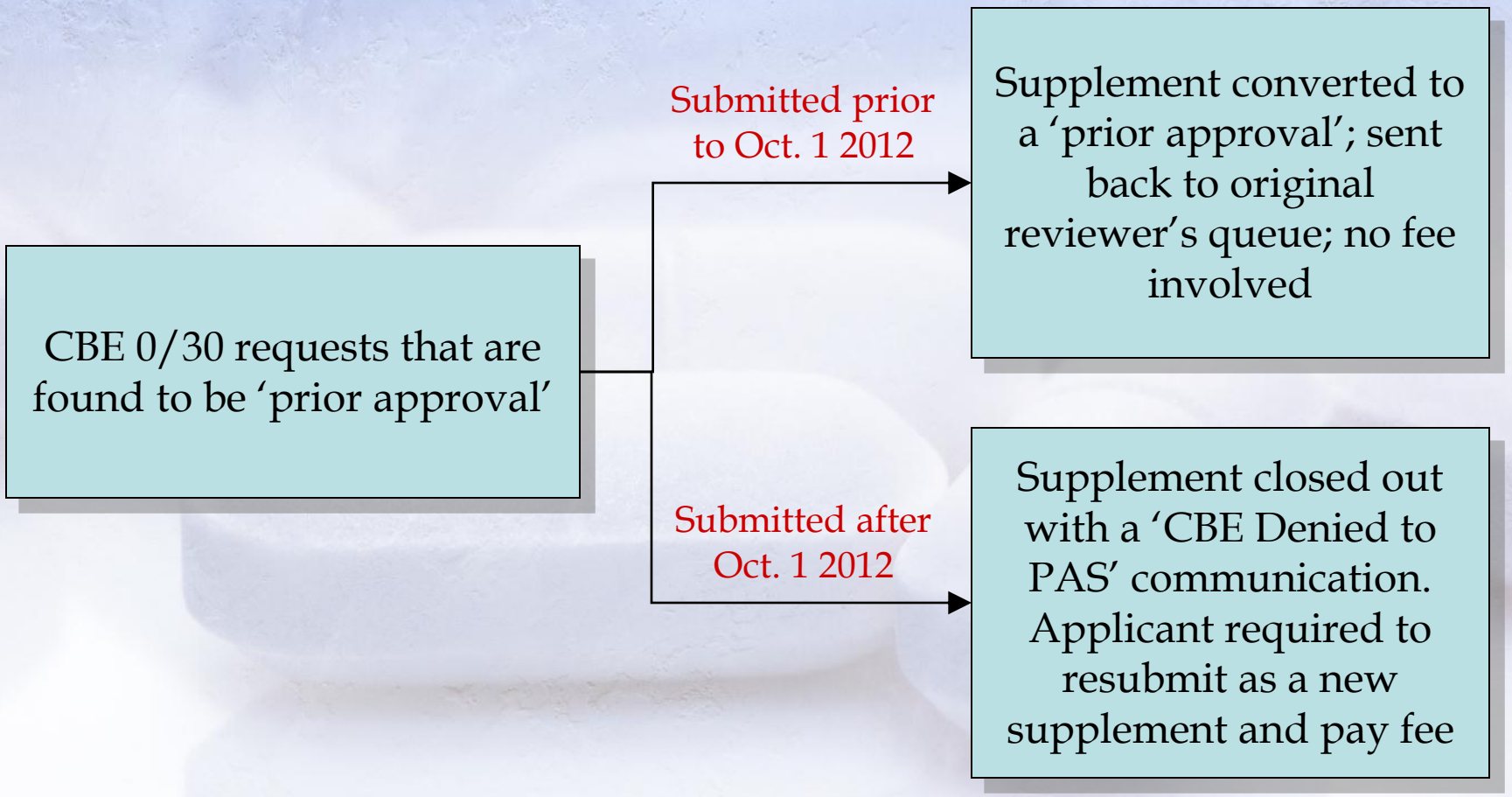
Changes to Supplements

Changes to Supplements

Fees apply to all post October 1, 2012 Prior Approval Supplements

- Chemistry, Labeling, Microbiology, Bioequivalence.
- If multiple changes or discipline reviews needed in PAS still only one fee.
- If submitting a grouped/global PAS change impacting multiple ANDAs, separate PASs needs to be submitted to each ANDA and applicable application fees for each separate ANDA submission should be paid.

Changes to Supplements (continued)



30 Minute Post First Complete Response (CR) Teleconference

30 Minute Post First CR Teleconference

- Goals established for FY ’15, ‘16 and ’17.
  - Will continue to honor requests in FY ’13 and ’14 at similar level as in pre-GDUFA.
  - Goals are minimums, we may conduct more
    - 200 in FY15, 250 in FY16, 300 in FY17
- Teleconference will be a 30 minute discussion to clarify issues and answer questions with respect to issued *First Cycle* Complete Response only.

30 Minute Post First CR Teleconference *(continued)*

- Request for teleconference should be received within 10 business days after issuance of first review complete response action from FDA/OGD.
- Request should to be a written request and submitted to the ANDA archival file.
- Request should outline all specific questions the applicant would like to discuss during teleconference.
  - Teleconference discussion limited to contents of the CR letter deficiencies only.

30 Minute Post First CR Teleconference *(continued)*

- Request should be clearly labeled as "*Post 1st Complete Response Telephone Meeting Request*".
- OGD will schedule teleconference as soon as possible.
  - based on availability of all parties that are required to participate.
- Priority given to expedited ANDA and ANDAs that received a 'First Major' Complete Response.


Teal
"Ok, now what?"

GDUFA is a 5 year plan

- Change does not happen quickly in the government
- FY2013 – CR and sequester
- Hiring, budget
  - OGD alone, 57 hires on board or in process
- Lots still to do……
- Please be patient

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Website: http://www.fda.gov/gdufa

Email: AskGDUFA@fda.hhs.gov

Call: (866) 405-5367